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EXAMINER	
KOLKER, DANIEL E	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 04/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/977,579	COX ET AL.	
	Examiner	Art Unit	
	Daniel Kolker	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *4-9,15,17-19,21-23 and 30-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,10-14,16,20 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-38* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 October 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 10/15/01, 4/5/02
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's response and remarks filed 15 February 2005 have been entered. Claims 1 – 38 are pending in the instant office action.

Election/Restrictions

2. Applicant's election with traverse of Group I, and SEQ ID NO:2 in the reply filed on 15 February 2005 is acknowledged. Group I is drawn to nucleic acids, but SEQ ID NO:2 is a polypeptide sequence. In a telephone conversation on 24 March 2005, Angela Collison elected SEQ ID NO:4, which is a nucleic acid sequence. A written reply confirming election of the specific sequence is requested.

The traversal is on the ground(s) that restriction between Groups I – VI is improper. Specifically, applicant argued that since Groups I, II, III, V, and VI are all classified in class 435, a thorough search of this class would be informative, and is required for search of nucleic acids. This is not found persuasive because a search of the *entire* class is neither necessary nor appropriate for examination of the elected nucleic acid sequence. Class 435 currently comprises over 79,000 patents and 39,000 pre-grant publications. Searching the nucleic acid sequence would involve both a search of the relevant databases and some classes (for example, vectors, which are classified in class 435, subclass 320.1). However other subclasses are beyond the scope of the present search including, for example, subclass 183, enzymes, which comprises over 1800 patents and 3000 pre-grant publications. Clearly a search of class 435 as a whole is not necessary. Therefore doing so would be a serious burden.

Applicant further argues that Groups I – III are all related to nucleic acids, and therefore should be examined together. However, Group I is drawn to nucleic acids, whereas Groups II and III are drawn to methods of using nucleic acids. Restriction between products and processes of using those products is proper (see MPEP § 806.05 (h)), and since the methods of using the nucleic acids require search beyond the nucleic acid databases (e.g. in the patent and non-patent literature to evaluate the novelty of the claimed methods, as opposed to the novelty of the products), search of Groups II and III is not co-extensive with search for Group I.

Applicant further argues that for search and examination purposes, selection of a single nucleic acid sequence should have been an election of species rather than a further restriction requirement. Each sequence must be searched independently in both commercial (e.g. EST, GenBank) and patent (e.g. all issued patents, all pre-grant publications, and all WIPO patent

publications) databases. Searching of nucleic acid sequences is particularly burdensome on the office's resources. As set forth in the restriction requirement mailed 15 December 2004 (see specifically p. 6), each nucleic acid sequence is patentably distinct and has different chemical and physical characteristics, and requires a separate search.

No groups or additional sequences will be searched.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 4 – 9, 15, 17 – 19, 21 – 23,and 30 – 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 15 February 2005.

4. Claims 1 – 3, 10 – 14, 16, 20, and 24 – 29 are under examination in the instant office action.

Drawings and Sequence Compliance

5. The disclosure is objected to because of the following informalities:

Drawings which include nucleic or amino acid sequences must include the appropriate SEQ ID NO: in either the drawing or the Brief Description of the Drawings. See MPEP § 2422.02.

Claim 14 refers to specific nucleotide sequences which are referred to by accession number rather than SEQ ID NO:. All sequences in patent applications must be referred to by SEQ ID NO:. See MPEP § 2422.03.

Appropriate correction is required.

Claim Rejections - 35 USC §§ 101 and 112

6. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1 – 3, 10 – 14, 16, 20, and 24 – 29 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to novel polynucleotides, vectors and host cells comprising same, kits, and methods of purifying polypeptides from said host cells. The specification asserts that the polynucleotides have the following uses, none of which are specific and substantial. To the extent that the polynucleotides encode polypeptides, the utility of the polypeptides themselves must be considered.

1) The polynucleotides encode polypeptides which are themselves useful, because they are sodium channel subunits. It is acknowledged that the polypeptides encoded by the polynucleotides, when placed into cells, appear to be functional in sodium channels, as detailed in Examples 6 and 7. However, this is not a specific and substantial utility. Applicant has not demonstrated why one would want to *use* the beta-3 subunit encoded by the polynucleotides. There is not a nexus between a specific disease or condition and the instantly-claimed beta-3 subunits. In order for a utility to be substantial, it must define a real-world use. See MPEP § 2107.01.

2) The encoded polypeptides are useful as targets of drugs capable of either up- or down-regulation of voltage-gated sodium channels, or in the identification of modulators or ligands (specification, p. 36). Applicant has listed several diseases on p. 7 which may be affected by the instantly claimed polynucleotides and polypeptides, and asserts that the polynucleotides and encoded polypeptides are useful as targets for drugs related to these diseases. This utility is neither specific nor substantial. Any protein could be a target for drugs; therefore the asserted utility is not specific. Applicant has listed several diseases in which beta-3 subunits may play a role (p. 7), but mere speculation as to the involvement of a molecule in a disease or condition is not a substantial utility. Applicant is again directed to See MPEP § 2107.01, which states: "A "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities." Clearly significant further research is needed in order to determine if the instantly claimed polypeptides or polynucleotides are in fact associated with any of the diseases listed by applicant on p. 7 of the specification.

3) The polynucleotides can be used to detect or isolate similar sequences, i.e. in hybridization assays (specification, p. 13). This utility is not specific since it can be performed

with any polynucleotide. Furthermore it is not substantial, as methods of detecting molecules for which there is no use does not constitute a substantial utility. See MPEP § 2107.01, particularly the section titled "Substantial Utility".

4) The polypeptides can be used to make antibodies (specification, p. 20). This utility is not specific as it can be performed with any polypeptide. Furthermore it is not substantial, as there is no reason to make an antibody, either for purifying or for detecting beta-3 subunits. Methods of purifying or detecting molecules for which there is no use do not constitute substantial utilities.

5) The polynucleotides themselves are useful as therapeutics (specification, p. 26). As mentioned above, applicant has not demonstrated a nexus between the instantly claimed molecules and any disease or condition. In order to use the polynucleotides as therapeutics, significant further research would have to be performed. For example, one would first have to identify a disease in which the polynucleotide is either mutated or deleted, and then design a therapeutic regimen to use the polynucleotides. While there is little doubt that such a use may be important, the efforts involved therein constitute invention, and the act of invention is not complete until a nexus between the molecule and a disease or condition has been made.

6) The polynucleotides are useful because they hybridize near disease markers on chromosome 11. The specification discloses (p. 4, lines 20-31) that the genes for human N-CAM and the beta-2 sodium channel are close to the chromosomal region to which the instantly claimed polynucleotides have been mapped. This is not a substantial utility. The teachings of Pericak-Vance (1996. Current Protocols in Human Genetics 1.4.1 – 1.4.31) are particularly informative. Pericak-Vance teaches that markers are necessary for mapping of disease traits, and that a desirable spacing of markers is 10 to 20cM (p. 1.4.7, first column). Applicant has not disclosed the genetic distance between the instantly claimed polynucleotides and any other markers, hence it is not clear that the polynucleotides are useful in mapping studies. Pericak-Vance further teaches that before a marker is to be used, estimates of allele frequency should be obtained from at least 100 control individuals (p. 1.4.7, first column), and that markers must be polymorphic in order to be useful (p. 1.4.10, second column). Furthermore, informativeness of a marker depends on both the number of alleles at the locus containing the marker and the relative frequencies of those alleles in the population at large (p. 1.4.16, second column). The limited information provided by applicant, i.e. that the instantly claimed polynucleotides hybridize

close to known human genes which, does not confer a substantial utility in light of what is known to constitute a useful marker.

8. Claims 1 – 3, 10 – 14, 16, 20, and 24 – 29 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9. Even if claims 1 – 3, 10 – 14, 16, 20, and 24 – 29 had utility, enablement would not be commensurate in scope with the claims. The specification does not reasonably provide enablement for sequences identified only by name (i.e. as in claim 1, which recites "a beta3 subunit from a voltage-gated sodium channel"), or sequences which are less than 100% identical to SEQ ID NO:4 (i.e. claim 10, drawn to sequences at least 90% identical to SEQ ID NO:4), or the use of host cells in gene therapy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

The claims are drawn to isolated nucleic acids, vectors and host cells comprising same, kits, and methods of purifying polypeptides from said host cells. Claims 1 – 3 are broad in that they do not require that the claimed polynucleotides have any particular sequence. A skilled artisan would not be able to make the polynucleotides of claims 1 – 3, as there is no guidance given as to what constitutes a beta3 subunit. There is variation across species, and the descriptive identification alone is not sufficient to permit construction or isolation of the nucleic acids.

Claims 10 and 11 are drawn to isolated nucleic acids defined only by sequence identity to SEQ ID NO:4 or a portion thereof. There is no requirement that the nucleic acids encode a protein with any particular function. There is no guidance as to which regions of SEQ ID NO:4 must be preserved when making changes, nor is there guidance as to where additions,

insertions, deletions, or substitutions can be made. Claims 14 and 16 are drawn to any 10 nucleotides of a nucleic acid that encodes a beta-3 subunit; again there is no guidance as to which regions must be conserved, or any requirement that the 10 nucleotides have any function.

Claim 20 recites "a pair of amplification primers" but guidance is not given as to what constitutes an amplification primer. There is no guidance as to whether said primers should be DNA, RNA or some other chemical, or how long they should be, or where on the sequences of the nucleic acids of claims 1 – 17 they should bind.

Claim 28 is drawn to a recombinant host cell. The specification (pp. 24 – 27) clearly contemplates the use of the claimed nucleic acids in gene therapy applications. The broadest reasonable interpretation of the term "recombinant host cell" recited in claim 28 includes cells residing in a human body which have been infected, transformed, or transfected with the instantly claimed nucleic acids. The state of the art of gene therapy is unpredictable. Those skilled in the art recognize that such technology is currently beyond scope. In particular, Marshall "Gene Therapy's Growing Pains". Science, Vol. 269 (1995), pp. 1050-1055, Orkin et al. "Report and recommendations of the panel to assess the NIH investment in research on gene therapy". (1995). pp. 1-39, and Verma, I. M., et al. "Gene therapy-promises, problems, and prospects". Nature, Vol. 389 (September 1997), pp. 239-242, each denote significant troubles associated with *in vivo* gene therapy approaches to the assessment of *in vivo* methods and treatments. The specification fails to provide any working examples of gene therapy methods. Since the scope of "cell" is deemed to be so inclusive as provided by direct guidance within the specification, the scope of enablement provided by the specification is not commensurate in scope with the claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986). Thus, the skilled artisan cannot readily make and use the claimed sequences without further undue experimentation. Amendment to "isolated recombinant cell" is recommended.

The nature of the invention, nucleic acids that encode voltage-gated sodium channels, is complex. The prior art indicates that even subtle changes in sequence of mammalian voltage-gated sodium channels can result in large-scale changes in their function. Wallace et al. (1998.

Nature Genetics 19:366 – 370) teach that a single base-pair change in a beta-1 subunit of a voltage-gated sodium channel leads to significant changes in channel kinetics (see Figure 5), a loss-of-function allele (see abstract) and to epilepsy (see whole paper).

Because the claims are broad, the nature of the invention is complex, there is little guidance in the specification as to where changes can be made, and the prior art indicates that even single-nucleotide changes can result in loss of function, it would not be possible to make and use the invention commensurate in scope with the claims.

10. Claims 1 – 3, 10 – 14, 16, 20, and 24 - 29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1 – 3 do not recite any specific sequence, but rather only the name of a gene. Furthermore claims 1 – 3 are drawn to any nucleic acid sequence, not limited by length, structure, or function, that is complementary to any portion of the unspecified sequences. Claims 10 – 11 only require a certain percent sequence identity, but do not require that any specific element be retained, and the specification does not fully describe the large genus claimed (i.e. all possible sequences, including deletions, insertions, or substitutions anywhere along the sequence such that 90% identity is retained). Claims 12 and 13 only require that the nucleic acid comprise two specific residues; they do not require that the nucleic acids comprise the entire sequence between those referred to as the starting and ending points. Amendment to "wherein said nucleic acid comprises residues 1 – 375 of SEQ ID NO:4" (claim 12) and "wherein said nucleic acid comprises residues 1024 – 1261 of SEQ ID NO:4" (claim 13) is suggested. Claims 14 and 16 are drawn to any 10 nucleotides of a sequence, but again do not recite the actual sequences that applicant is attempting to claim, and as stated previously the specification does not describe the full genus claimed.

The claims are akin to example 6 of the Revised Interim Written Description Guidelines Training Materials, available on the USPTO'S web site at http://www.uspto.gov/web/offices/pac/writtendesc.pdf, directed to the recitation of genes. The claims are drawn to genera of nucleic acid sequences, including those with regulatory elements, untranslated regions, allelic variants, mutation sequences, and sequences across mammalian species as encompassed by the terms "beta3 sub-unit from a voltage-gated sodium channel".

No sequence is recited in claims 1 - 3. The art teaches that the interactions of untranslated regions of genes is complex and gene-specific (see Mazumder et al., 2003. Trends in Biochemical Sciences 28:91-98, particularly the paragraph that spans pp. 91 - 92). One of skill in the art would not be able to know, based on the disclosure, which elements are necessary for the construction of the agents claimed herein.

Claims 1 – 3, 10 – 11, 14, 16, 20, and 24 – 29 are drawn to polynucleotides which encode a beta-3 subunit of a voltage-gated sodium channel, but applicant has given only two examples, namely SEQ ID NO:s 3 and 4, which encode the rat and human beta-3 subunits (specification, p. 7, lines 15 – 19). The instant disclosure of two nucleic acid sequences cannot support description of the entire genus of polynucleotides, which encompass a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA or protein, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id at 1170, 25 USPQ2d at 1606." The instant disclosure does not provide adequate written description for the genera and sub-genera of the claims.

Claim 20 recites "a pair of amplification primers" but neither the claim nor the specification defines what constitutes an amplification primer. There is no requirement that the primer be of any particular chemical structure, length, or nucleic acid sequence. There is no requirement that it bind to any particular part of any of the nucleic acids in claims 1 – 17.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 14, 16, and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Fleishmann et al. (U.S. Patent 6,294,328, issued 25 September 2001, filed 24 June 1998). The claims are drawn to nucleic acids comprising at least 10 consecutive nucleotides of a nucleic acid encoding a beta-3 subunit. Fleishmann et al. teach SEQ ID NO:2. Nucleotides 7364 – 7383 of Fleishmann et al. are complementary to nucleotides 500 – 519 of instantly claimed SEQ ID NO:4. Because the prior art sequence is complementary to the claimed sequence, the two will inherently hybridize under stringent conditions. While applicant has provided a definition of stringent conditions on p. 11 of the specification, that definition is exemplary, not limiting, and thus the term can include conditions of any stringency. Therefore the prior art sequence meets the limitations of claim 24.

13. Claims 14, 16, 20, 24, and 26 - 29 are rejected under 35 U.S.C. 102(e) as being anticipated by Lovenberg et al. (U.S. Patent 6,723,841, issued 20 April 2004, effective filing date 7 June 1995). Lovenberg et al. teach SEQ ID NO:3. Bases 95 – 113 of SEQ ID NO:3 are identical to bases 72 – 90 of instantly claimed SEQ ID NO:4. Claim 20 is drawn to a kit comprising a pair of primers capable of hybridizing to a beta3 subunit nucleic acid, including those of claims 14 and 16, plus printed material. However inclusion of nonfunctional printed

matter does not make a product patentable over the prior art (see MPEP § 2112.01, final paragraph). Loveneberg et al. teach a sequence that meets the limitations of claims 14 and 16 as described above and teach methods of designing primers (column 26 lines 36 – 55); therefore the prior art teachings of Lovenberg also anticipate claim 20. Applicant has defined nucleic acids to include double-stranded nucleic acids (specification, p. 9, lines 17 – 19), thus the sequence from Lovenberg et al. will inherently hybridize to the claimed nucleic acid, meeting the limitation of claim 24. Lovenberg et al. teach labeling their nucleic acids with detectable labels (column 24, line 51 – column 25, line 5). Lovenberg et al. teach vectors comprising their sequence and host cells comprising said vectors (column 12, line 9 – column 16, line 5), meeting the limitations of claims 27 and 28. Lovenberg et al. also teach methods of producing the encoded polypeptide recombinantly (column 17, lines 4 – 19), meeting the limitations of claim 29.

14. Claims 14, 16, and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by GenBank Locus D44825. This sequence was first made public 29 September 1996. Bases 33 – 170 of D44825 are 100% identical to bases 1044 – 1181 of instantly claimed SEQ ID NO:4, and bases 172 – 248 of D44825 are 100% identical to bases 1183 – 1259 of SEQ ID NO:4. The prior art sequence meets the limitations of claims 14 and 16. For the same reasons stated above, the sequence also meets the limitations of claim 24.

15. Claims 1 – 3, 10, 16, 20, 24, and 27 – 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Stratagene random primers, 1991 catalog, p. 66.

Stratagene teaches the use of random 9-mers capable of hybridizing with all possible gene sequences. The random primers meet the claim limitations because the primers are a complement to SEQ ID NO:4 and are able to bind under stringent hybridization conditions as the activity of extension exemplified is dependent upon hybridization of the random primer sequences. As noted in the catalog the primers and included reagents are capable of generation 500-1000 nucleotide segment primer copies. Thus, the reference teachings anticipate the claimed invention.

Claim Rejections - 35 USC § 103

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

> the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

17. Claims 1 – 3, 10, 14, 16, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fleishmann et al. in view of Brown et al. (U.S. Patent 5,807,522, issued 15 September 1998, filed 7 June 1995), or in the alternative Lovenberg et al. in view of Brown et al., or in the alternative D44825 in view of Brown et al., or in the alternative Stratagene in view of Brown et al. The claims are drawn to isolated nucleic acids, kits comprising same, and nucleic acids immobilized on a substrate. Fleishmann, Lovenberg, and D44825 teach nucleic acids that meet the limitations of claims 14 and 16, as described in detail in the rejections under 35 USC 102 above. Stratagene teaches nucleic acids which meet the limitations of claims 1 – 3. 10, 14, 16, and 24. Neither Fleishmann nor Lovenberg nor D44825 nor Stratagene teach nucleic acids immobilized on a substrate.

Brown et al. teach nucleic acids immobilized on glass slides ("microarrays", see column 14, lines 1 – 34), meeting the limitation of claim 24. Brown et al. also teach that microarrays are particularly useful for a number of applications, including gene mapping and genetic diagnostics (column 14, lines 43 – 60). It would have been obvious to one of ordinary skill in the art to immobilize the nucleic acids of either Fleishmann, Lovenberg, Stratagene, or D44285 on a substrate, with a reasonable expectation of success. A motivation would be to map genes or to diagnose diseases, and is provided by Brown.

Brown et al. also teach labeled nucleic acid probes (column 15, lines 5 – 18), meeting the limitations of claim 25. Brown et al. teach that labeled probes are useful for monitoring gene expression in different cell types, disease states, responses to drugs, and responses to environmental factors. It would have been obvious to one of ordinary skill in the art to label the nucleic acids of either Fleishmann, Lovenberg, Stratagene, or D44285 with a detectable

molecule, as taught by Brown, with a reasonable expectation of success. The motivation would be to monitor gene expression, as suggested by Brown.

Double Patenting

18. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

19. Claims 1 – 3, 10 – 14, 16, 20, and 24 – 28 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 10 – 13, 17, 20, and 24 - 28 of copending Application No. 09/936,680. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons:

Claims 1 – 3 of the instant application are drawn to the genus of nucleic acids encoding beta-3 subunits of voltage-gated sodium channels. Dependent claims 10 – 14 are drawn to nucleic acids at least 90% identical to SEQ ID NO:4, or to nucleotides 1 – 375, 376 – 1023, 1024 - 1261 of same, or at least 10 consecutive nucleotides of a beta-3 subunit. Claims 10 – 14 of the '680 application recite the same verbiage, although they depend from a narrower base claim (claim 5, drawn to nucleic acids encoding beta-3 subunits at least 80% identical to SEQ ID NO:2). Claim 16 of the instant application is drawn to any 10 nucleotides of SEQ ID NO:4; claim 17 of the '680 application recites certain specific SEQ ID NO:s that meet this limitation.

Instant claim 20 is drawn to a kit comprising a pair of primers which can hybridize to any of the nucleic acids in claims 1 – 17; claim 20 of the '680 application is drawn to a kit comprising a pair of primers encoding specific SEQ ID NO:s which meet this limitation.

Claims 24 – 28 of the instant application are drawn to kits for detecting the presence of polynucleotides, vectors, and host cells. Claims 24 – 28 of the '680 application recite very similar verbiage, although they are depend from base claims with narrower scope than those of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

20. No claim is allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on (571) 272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Daniel E. Kolker, Ph.D.
April 26, 2005

SHARON TURNER, PH.D.
PRIMARY EXAMINER
4-27-05